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Balloon Angioplasty Results in Increased Segmental Coronary Distensibility: A Likely Mechanism of Percutaneous Transluminal Coronary Angioplasty

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Objectives. The purpose of this study was to evaluate the hypothesis that the increase in lumen area induced by percutaneous transluminal coronary angioplasty is secondary to a change in lesion (segmental) distensibility.

Background. Despite the widespread use of coronary angioplasty, the precise mechanism (or mechanisms) of lumen area improvement remains poorly understood.

Methods. Quantitative coronary angiography was used to measure the minimal (contrast agent filled) balloon diameters at 1 to 5 atm, inclusive, during the first and final balloon inflations in 24 lesions successfully treated with coronary angioplasty. To rule out possible confounding effects due to changes in balloon material distensibility during repeated inflations, five control balloons were studied ex vivo. In parallel, intravascular ultrasound imaging was utilized to compare the segmental distensibility (change in lumen area during the cardiac cycle) of eight disease-free and seven mildly diseased coronary segments and seven segments after successful balloon angioplasty.

Results. Minimal balloon diameters increased significantly between the first and final inflations (46%, 33%, 26%, 14% and 10% at 1, 2, 3, 4 and 5 atm, respectively, all $p < 0.0001$), demonstrating an increase in arterial distensibility after successful coronary angioplasty. No significant changes in balloon diameters were observed during sequential initial inflations at 1 and 2 atm ($n = 5$). Minimal increases in balloon diameters were observed during repeated balloon inflations in the ex vivo studies (4.9 ± 1% [mean ± SEM]). A distensibility index, derived from the intravascular ultrasound data, was not different between the balloon-dilated and the normal segments but was significantly lower in mildly diseased sites (14.7 ± 2.2 vs. 12.9 ± 1.2 vs. 6.9 ± 1.9, respectively, $p < 0.05$) despite a smaller plaque area (7.3 ± 1 vs. 11.3 ± 1 mm^2, proximal/nondilated vs. dilated segments, respectively, $p < 0.05$).

Conclusions. Coronary distensibility is significantly impaired in atherosclerotically diseased coronary segments and increases significantly after balloon angioplasty. This increase in segmental coronary compliance after coronary angioplasty may create a larger lumen area by allowing the vessel to distend in response to normal intraarterial pressure.

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The precise mechanism(s) of improvement in lumen cross-sectional area after successful percutaneous transluminal coronary angioplasty remains poorly understood. Early studies confirmed that plaque compression and extrusion and distal embolization play a minimal role in this process (1–3). Some animal and cadaver studies have suggested that irreversible medial injury with "aneurysmal" dilation might be a primary mechanism of lumen enlargement (4–7). More recently (8–10), it has been suggested that a large proportion of the increase in lumen cross-sectional area after coronary angioplasty is related to an increase in segmental coronary distensibility after the media is released from the cicatrizing effects of the noncompliant intimal plaque. This "release" of the media, secondary to plaque splitting, may allow the vessel to passively distend in response to hydrostatic forces (blood pressure).

This study was conducted to evaluate the effect of balloon dilation on segmental coronary distensibility. We used quantitative angiographic techniques to measure the degree of expansion of angioplasty balloons at the site of a coronary lesion during incrementally increasing inflation pressures during the first and final balloon inflations during coronary angioplasty. Comparison of the minimal balloon diameter at each sequential pressure during the two inflations provides a mean to quantify the change, if any, in segmental (lesion) coronary distensibility induced by coronary angioplasty. In an additional series of patients two consecutive inflations

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were performed at low pressure before proceeding to the usual dilating pressures in an attempt to further elucidate the mechanism of successful coronary angioplasty. To rule out the potentially confounding effects of increases in balloon material distensibility due to repeated inflations, control ex vivo studies were performed. Intravascular ultrasound studies were also performed in normal, mildly diseased and postangioplasty coronary segments to further assess the effect of coronary angioplasty and progressive degrees of atherosclerosis on segmental arterial distensibility.

Methods

Study patients. The full 1- to 5-atm inflation protocol, as described next, was performed in 24 lesions in 22 patients. A modified protocol with sequential low pressure (1 and 2 atm) inflations was performed in an additional five lesions in five patients. Patient inclusion criteria included single- or double-vessel disease, electively performed coronary angioplasty, reference vessel diameter ≥2.5 mm, discrete stenosis <100%, lesion length <15 mm and absence of angiographic evidence of thrombus. Patients were excluded if there was a need for a larger balloon than that used in the first inflation. Only patients with successful coronary angioplasty (residual stenosis <50% and Thrombolysis in Myocardial Infarction trial [TIMI] flow grade 3) were included. The protocol for this study was approved by the Institutional Review Board of the Stanford University Medical Center, and all patients gave informed consent before proceeding.

Coronary angioplasty procedure. Selective coronary angiography of the vessel to be dilated was performed in multiple projections using the 4- to 5-in. (10 to 13 cm) image cesium iodide intensifier mode at a cine rate of 30 frames/s. The projection that best demonstrated the target coronary lesion, minimizing vessel overlap and foreshortening, was chosen and used for all subsequent images. To avoid possible differences between different balloon materials or catheter types, all coronary angioplasty was performed using polyethylene 2.5- to 3.5-mm balloon catheters (ACX, Advanced Cardiovascular Systems, Inc.). Balloon size was chosen to match the lumen diameter of the adjacent angiographically "normal" reference segment. The balloons were prepared with undiluted contrast agent (Conray 60) to enhance radiographic visualization, paying special attention to eliminate all possible air bubbles. Intracoronary nitroglycerin (150 to 300 μg) was routinely administered before angioplasty and before final angiography. Once the guide wire was advanced distally beyond the target lesion, the balloon was advanced to the site of stenosis such that the central radiopaque balloon marker was positioned at the center of the lesion. The balloon was then sequentially inflated for the first time at 1, 2, 3, 4 and then 5 atm under continuous fluoroscopic observation. After a minimum of 10 s after each particular pressure was reached, or longer if there was any fluoroscopic evidence of further change in balloon size or contour, cineangiographic imaging of the contrast agent-filled balloon was obtained. All images were taken for each patient in an identical view, with the same degree of angulation, intensifier–patient distance and table height. Additional balloon inflations were then performed at the discretion of the operator until an angiographically satisfactory result was achieved. A final sequential inflation was performed with identical methodology as the first inflation, filming the balloon after each pressure (i.e., 1, 2, 3, 4 and 5 atm) was reached and full balloon expansion at each pressure was achieved. A final postprocedure angiogram with the balloon and guide wire withdrawn was obtained.

To further elucidate the mechanism of balloon angioplasty, five additional patients were studied with a slightly different protocol. In this series of patients two consecutive inflations were performed at low pressures only (1 and 2 atm) before proceeding with the actual angioplasty. A final sequential inflation at 1 and 2 atm was performed once a satisfactory result was achieved. The first two consecutive low pressure inflations were at pressures below that typically associated with the sudden increase in balloon diameter that is assumed to represent the splitting of the plaque. The final inflation was done after complete expansion of the balloon was achieved at higher inflation pressures and therefore would presumably reflect the distensibility of the arterial segment once the plaque was split.

Balloon control study. Five control ex vivo measurements of balloon distensibility were performed to examine the possible confounding effects of changes in balloon material distensibility with repeated inflations. Three 2.5-mm and two 3.0-mm balloon catheters (previously unused), identical to those used in the patients, were introduced into a plastic tray filled with warmed (37°C) normal saline solution via an 8F guide catheter that was filled with contrast agent for the purpose of calibration and magnification correction. Balloons were then inflated following the same methodology described earlier. Undiluted contrast agent (Conray 60) was used, and cineangiographic images of the balloon and guide catheter were recorded at 1, 2, 3, 4 and 5 atm during the first inflation. Balloons were then inflated twice to 8 atm for 1 min per inflation, and a final sequential inflation was performed with images obtained again at 1, 2, 3, 4 and 5 atm.

Angiographic analysis. Quantitative angiographic techniques were used to measure balloon diameters. The system employed utilizes automated computer-assisted edge detection of a digitized cine image and has been described elsewhere (11). Briefly, for every cineangiographic run obtained at the sequential first and final balloon inflations, two consecutive frames were selected and magnified 3.5 times, with the balloon centered in the image field. The image was then digitized (model 5524, De Anza Systems), with the video processor controlled by a 2100 computer (Hewlett-Packard). Magnification correction and calibration were achieved using the contrast agent-filled 8F coronary guide catheter. After the segment of interest was designated (the center 15 mm of the balloon), the computer generated

balloon boundaries and minimal and mean diameters were derived for each segment. Only minimal balloon diameters were used for subsequent data analysis because they were thought to best represent the balloon contact zone with the underlying diseased segment. In general, for a given lesion the waist or minimal dimension of the balloon occurred at the same site, but minimal diameter was objectively determined by a computer-assisted edge detection algorithm to ensure objectivity and was not necessarily at an identical site in the balloon in every case. The same methodology was used to analyze the reference vessel, the coronary lesion before and after coronary angioplasty and the control ex vivo balloon inflations. All measurements were performed in two consecutive frames (end-diastolic for the in vivo study). The data shown represent the average of these two measurements. All measurements were performed by the same investigator to minimize variability. The resolution of this system for coronary artery analysis has been demonstrated to be ±0.06 mm (11), with a (mean) frame to frame variation ~0.15 mm.

Intravascular ultrasound procedures. The procedure for intracoronary ultrasound image acquisition at our institution has been described elsewhere (12). Briefly, intravascular ultrasound images were provided by a 5F or 4.3F 30-MHz ultrasound catheter (CVIS Inc.). The catheter has a lumen that accommodates a 0.014-in. (0.036 cm) coronary guide wire that allows its manipulation in coronary arteries similar to balloon angioplasty systems. Images were recorded on ½-in. videotape for subsequent off-line analysis.

Intravascular ultrasound studies were performed in seven additional patients immediately after successful coronary angioplasty. Images of the balloon-dilated segment and of a mildly diseased proximal segment were recorded. In addition, as a control group, images were obtained at two coronary sites in four cardiac transplant recipients who had no evidence of coronary artery disease by either angiography or intracoronary ultrasound. Images of the balloon-dilated vessels (i.e., the dilated segment and the proximal mildly diseased segment) and the coronary arteries of the cardiac transplant recipients were subsequently digitized onto a 512 × 512 × 8-bit matrix in 34-frame sequences obtained at 30 frames/s by an image processing computer (Dextra Medical Inc.). The largest (systolic) and smallest (diastolic) lumens from the digitized cardiac cycle were obtained for analysis. The lumen–vessel interface and the external border of the intimal layer (i.e., intimal–medial interface) were traced by planimetry. This allows calculation of the "plaque" area in the proximal and balloon-dilated segments in the patients with coronary angioplasty (i.e., subtracting the lumen area from the area within the external border of the intimal layer) and the calculation of a fractional intimal area defined as the ratio of plaque area to the sum of the plaque and lumen areas. This is referred to as the plaque index. A distensibility index was calculated for each segment as the largest minus the smallest lumen area divided by the smallest lumen area multiplied by 100. A similar definition has been used by Gurley et al. (13). The data shown represent the average of three cardiac cycle measurements.

Statistics. All data are presented as mean value ± SEM. Comparisons between minimal balloon diameters during the first, second and final inflations were analyzed by one-way analysis of variance using repeated measures (Scheffé F test, Statview). Comparisons of intravascular ultrasound measurements between groups were performed using the Kruskal-Wallis test. Comparisons between two variables were performed using a Student unpaired t test or Mann-Whitney U test for continuous variables and the chi-square test for categoric variables. Analysis of scattergram plots was performed using a linear regression approach. Data are plotted as mean values for each group, with errors bars signifying ±SEM, and $p < 0.05$ was considered statistically significant.

Results

The patient and procedural data are shown in Table 1. Twenty-four lesions were studied in 22 patients. Single-vessel coronary angioplasty was performed in 21 patients and double-vessel angioplasty in 1. All of these lesions were new stenoses. In addition, one of the previously included lesions restenosed, and a second dilation was performed (lesion 3, Table 2) and included in the study. In one patient with an internal mammary artery bypass to the left anterior descending coronary artery, angioplasty of the "protected" left main coronary artery was performed. The average lesion length was 5.6 ± 0.4 mm. Nine lesions were classified as eccentric (lesion centerline in the outer 25% of the lumen). Nine of the lesions showed fluoroscopic calcifications, but in only four was the calcification graded as moderate or severe. No lesion was on a bend >45°, and no angiographic evidence of thrombus was observed before or after coronary angioplasty. A 2.5-mm balloon was used in 14 lesions, a 3.0-mm balloon in 8 and a 3.25- and 3.5-mm balloon in 1 each. The result was successful (<50% residual diameter stenosis and TIMI flow grade 3) in all lesions. Clinically insignificant intimal dissections were observed in six patients. There was no abrupt vessel closure or emergency coronary artery bypass surgery.

Balloon measurements of lesion distensibility. Minimal balloon diameters at each sequential pressure during the first and final in vivo inflations are shown in Table 2. In Figure 1, the minimal diameter of the balloon at each sequential pressure is plotted for the first and final inflations. At all pressures (1 to 5 atm), there was a significant increase in the minimal balloon diameter achieved after coronary angioplasty. The increase in minimal balloon diameter was greatest at low inflation pressures (46% at 1 atm [1.24 to 1.81 mm], 33% at 2 atm [1.48 to 1.97 mm], 26% at 3 atm [1.67 to 2.11 mm], all $p < 0.0001$). Although the increase diminished at higher pressures, it remained statistically significant (14% increase at 4 atm [1.95 to 2.21 mm], 10% increase at 5 atm [2.08 to 2.29 mm], $p < 0.0001$). Therefore, a consistently

Table 1. Patient and Procedural Data

Pts/lesions	22/24
Gender (M/F)	17/5
Age (yr)	60.8 ± 2.4
Range	28–80
Vessel dilated	
LMCA	1
LAD	9
LCx	6
RCA	8
Concentric vs. eccentric	15 vs. 9
Lesion length (mm)	5.6 ± 0.4
Range	3–10
Balloon size (mm)	
2.5	14
3.0	8
3.25	1
3.5	1
No. of inflations	3.9 ± 0.2
Inflation time (s)	340 ± 32
Max inflation pressure (atm)	7.7 ± 0.4
Min lesion diameter pre-PTCA (mm)	0.77 ± 0.05
% Stenosis pre-PTCA	73 ± 2
Min lesion diameter post-PTCA (mm)	1.93 ± 0.04
% Stenosis post-PTCA	21 ± 2

Values presented are mean value ± SEM or number. F = female; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LMCA = left main coronary artery; M = male; Max = maximal; Min = minimal; PTCA = percutaneous transluminal coronary angioplasty; Pts = patients; RCA = right coronary artery.

larger minimal diameter was achieved during the final balloon inflation at each pressure. This upward shift in the pressure–diameter curve is consistent with an increase in coronary segment distensibility, analogous to what has been proposed for the pressure–volume relation of the left ventricle (14). Figure 2 shows an angiographic example of increased segmental coronary distensibility after successful coronary angioplasty.

An attempt was made to measure the intrinsic distensibility of the coronary segment undergoing dilation by determining the pressure needed during the first in vivo inflation to reach two-thirds of the diameter achieved at 5 atm during the ex vivo control inflation. In Figure 3 the pressure at which the balloon achieved two-thirds of control balloon diameter at 5 atm is plotted against the minimal baseline diameter of the lesion. Using this measure of intrinsic distensibility there was a significant correlation between the lesion baseline severity and distensibility ($r = -0.527$, $p < 0.05$). Only 21 lesions are plotted because in two cases a balloon >3.0 mm was used for which no control balloon data was available, and in one lesion even at 5 atm the balloon diameter during the first inflation was less than two-thirds of the control balloon diameter.

The influence of eccentricity on distensibility measurements was also analyzed. No significant differences were observed between angiographically eccentric and concentric lesions in intrinsic distensibility measurements (2.9 ± 0.3 vs.

Table 2. Minimal Balloon Diameter Before and After Angioplasty and During First and Final Inflations

Lesion No.	Balloon size (mm)	Pre (mm)	1 atm		2 atm		3 atm		4 atm		5 atm		Post (mm)
			First (mm)	Final (mm)	First (mm)	Final (mm)	First (mm)	Final (mm)	First (mm)	Final (mm)	First (mm)	Final (mm)	
1	3.0	0.82	1.06	2.02	1.28	2.11	1.31	2.25	1.77	2.50	1.90	2.59	1.85
2	2.5	0.47	0.84	2.01	1.48	2.33	1.81	2.40	2.13	2.41	2.14	2.30	1.71
3	2.5	0.80	1.06	1.94	1.35	2.00	1.60	2.01	2.00	2.05	2.24	2.21	2.05
4	2.5	0.76	0.94	1.71	0.94	1.74	1.03	1.83	1.77	1.98	1.89	2.10	1.85
5	2.5	0.33	1.03	1.49	1.06	1.60	1.14	1.78	1.64	1.96	1.69	2.09	1.91
6	3.0	0.57	0.97	1.90	1.08	2.12	1.25	2.17	2.12	2.36	2.12	2.49	1.91
7	2.5	0.83	1.58	1.95	1.57	2.19	1.69	2.25	2.03	2.32	2.32	2.34	1.99
8	2.5	1.14	1.65	1.72	1.63	1.81	1.76	2.11	1.73	2.03	2.03	2.11	1.65
9	2.5	1.38	2.10	2.23	2.03	2.10	2.10	2.33	2.17	2.33	2.31	2.31	2.18
10	2.5	0.97	1.55	1.86	1.83	1.95	1.89	2.09	1.95	2.24	2.07	2.30	2.08
11	3.0	1.35	1.80	2.36	1.99	2.44	2.25	2.46	2.50	2.70	2.45	2.65	2.02
12	2.5	0.81	1.51	1.86	2.03	1.97	2.02	2.20	2.20	2.31	2.28	2.29	1.94
13	3.0	0.89	1.31	1.66	1.51	1.92	1.66	2.07	1.91	2.14	2.09	2.23	1.86
14	2.5	0.38	0.73	1.57	0.99	1.62	1.17	1.78	1.25	1.87	1.38	1.92	1.89
15	3.2	0.68	1.28	1.99	1.60	2.15	1.95	2.27	2.30	2.42	2.43	2.56	2.05
16	3.0	0.73	1.03	1.54	1.72	1.84	1.82	2.03	2.07	2.18	2.16	2.32	1.89
17	2.5	0.89	0.91	1.32	1.30	1.67	1.66	1.79	1.78	1.89	1.89	2.04	1.80
18	2.5	0.64	0.99	1.49	1.05	1.55	1.56	1.74	1.61	1.81	1.66	1.87	1.40
19	3.0	0.34	1.28	2.03	1.43	2.09	1.67	2.16	1.97	2.22	2.06	2.29	1.95
20	2.5	0.73	0.86	0.98	1.14	1.43	1.31	1.48	1.46	1.67	1.88	1.94	1.73
21	2.5	0.86	1.12	1.46	1.21	1.82	1.26	2.00	1.82	2.15	1.89	2.22	1.88
22	3.5	0.91	1.61	2.34	1.86	2.46	2.12	2.61	2.32	2.61	2.52	2.71	2.24
23	3.0	0.64	1.05	1.92	1.81	2.20	1.88	2.28	2.23	2.39	2.36	2.48	2.23
24	3.0	0.75	1.44	2.00	1.69	2.27	1.83	2.58	2.06	2.63	2.28	2.68	2.20

Pre = baseline minimal lesion diameter; Post = minimal lesion diameter after coronary angioplasty.

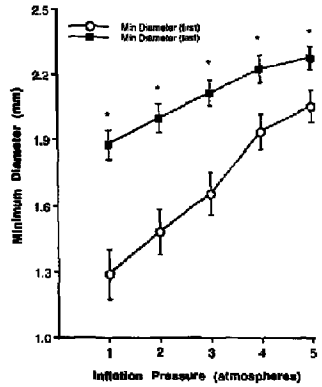

Figure 1. Line graph showing the relation between inflation pressure and minimal balloon diameter during the first and final balloon inflations (n = 24). A significant increase in diameter was achieved during the final inflation at all inflation pressures, suggesting an increase in segmental (lesion) distensibility after coronary angioplasty. The inflection in the distensibility curve between 3 and 4 atm during the first inflation may reflect the initial effects of plaque splitting, often discernible during fluoroscopy, caused by these higher pressure inflations. Values shown are mean values ± SEM at each inflation pressure. *$p < 0.0001$ for change in minimal balloon diameter (Min Diameter) between first and final balloon inflations.

3.1 ± 0.4 atm for eccentric and concentric lesions, respectively, p = NS). Similarly, the increment in minimal balloon diameters between the first and last inflations (33.8 ± 4.8% vs. 25.6 ± 2.5% mean increase for eccentric and concentric lesions, respectively, p = NS) were not significantly different for eccentric versus concentric lesions.

To further elucidate the mechanism by which distensibility is increased by angioplasty, a separate cohort of five patients underwent a different balloon inflation protocol. In these patients two consecutive inflations were performed at low pressures (1 and 2 atm), and a final sequential inflation (i.e., 1 and 2 atm) was performed once a satisfactory result was achieved. The results are summarized in Figure 4. No significant increase in minimal balloon diameter was noted during the second inflation compared with the first inflation. However, there was a large increase in balloon diameter ($p < 0.001$) during the final inflation at both 1 atm (0.78 ± 0.07 vs. 0.87 ± 0.07 vs. 1.93 ± 0.08 mm, respectively) and 2 atm (0.87 ± 0.07 vs. 0.91 ± 0.08 vs. 2.03 ± 0.07 mm, respectively).

Balloon distensibility measurements. To rule out the possible confounding effects of changes in balloon distensibility with repeated inflations, intrinsic balloon distensibility was evaluated in an ex vivo model. The control studies showed minimal changes in balloon diameter between the first and fourth inflations. Mean increases in minimal diameter of only 4.7 ± 0.9% (2.5-mm balloon) and 5.2 ± 0.6% (3.0-mm balloon) were observed between the first and final inflations. The increase in minimal diameter between first and final inflations was modestly greater at the higher inflation pressures (3.9%, 2.9%, 5.1%, 6.1% and 6.2% at 1, 2, 3, 4 and 5 atm, respectively).

Intravascular ultrasound measurements of distensibility. Intravascular ultrasound measurements at the balloon-dilated and proximal mildly diseased sites in patients with coronary angioplasty and at the control (normal) sites in cardiac transplant recipients are shown in Table 3. The distensibility index was significantly greater at the dilated site than at the proximal mildly diseased site of the same vessel (14.7 ± 2.2 vs. 6.9 ± 1.9, respectively, $p < 0.05$), despite a significantly larger plaque area (11.3 ± 1 vs. 7.3 ± 1 mm^2, $p < 0.05$) and plaque index (0.62 ± 0.03 vs. 0.36 ± 0.04, $p < 0.05$) at the dilated site. Distensibility measurements in transplant coronary arteries without any intimal thickening were not significantly different from those observed in the balloon-dilated sites but were significantly greater than in mildly diseased proximal segments (12.9 ± 1.2 vs. 6.9 ± 1.9, respectively, $p < 0.05$).

Discussion

This study demonstrates that segmental (lesion) coronary distensibility increases significantly after balloon angioplasty. It follows that a significant proportion of the increase in lumen cross-sectional area after coronary angioplasty may be secondary to an increase in segmental coronary compliance secondary to plaque splitting, which then allows the vessel to passively distend in response to hydrostatic forces (intraarterial blood pressure).

Mechanism of coronary angioplasty. Although angioplasty has been used to treat arterial stenosis for more than a decade, the mechanism of lumen enlargement after balloon dilation remains controversial. Before balloons were introduced and angioplasty was performed using progressively larger dilators, Dotter and Judkins (15) formulated the hypothesis of plaque redistribution and compression as the main mechanism of angioplasty. This hypothesis was also considered a likely mechanism of balloon angioplasty during the early years of this technique. However, atheromatous material has been shown to be relatively incompressible (1). Early studies demonstrated that the former proposed mechanisms as well as plaque extrusion or distal embolization play a minimal role in angioplasty-induced lumen enlargement (1–3). Animal and necropsy pathologic studies showed that cracking and splitting of the atherosclerotic plaque was a consistent finding after coronary angioplasty (5,6,16–18). It was then hypothesized that once the plaque was fractured, the balloon could stretch the muscle fibers, increasing lumen diameter. It was proposed that overstretching the vessel wall

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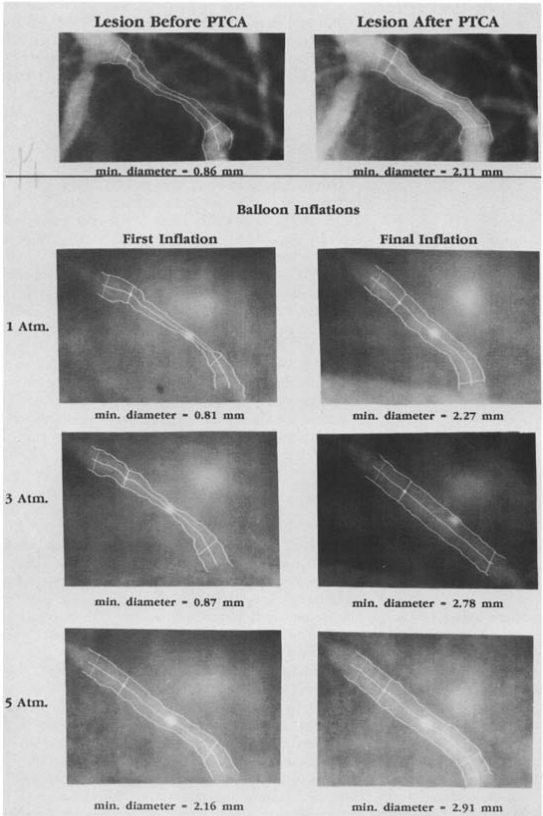

Figure 2. Angiographic demonstration of increased segmental coronary distensibility after successful coronary angioplasty. Top frames show the left anterior descending coronary artery lesion before and after coronary angioplasty. Angiographic frames of balloon inflation are shown at 1, 3 and 5 atm during the first and final balloon inflations.

beyond the limits of elasticity would induce medial injury, with smooth muscle paralysis and resultant aneurysm formation (6,7). This hypothesis, which was based primarily on observations from animal models and cadaver experiments, has become one of the more widely quoted mechanisms of coronary angioplasty. However, some clinical as well as experimental data appear to contradict this hypothesis. First, according to this theory one would expect a complete or nearly complete paralysis of the arterial wall once coronary angioplasty is performed. On the contrary, clinical studies have not uncommonly reported coronary artery spasm at the dilated site (19–24) or enhanced reactivity to vasoconstricting stimuli (25). In addition, we have previously observed that spontaneous coronary artery vasoconstriction occurs nearly routinely after coronary angioplasty at the dilated site (24,26,27). Moreover, the degree of stretch of the arterial wall normally induced by angioplasty does not seem to be sufficient to produce irreversible muscle cell

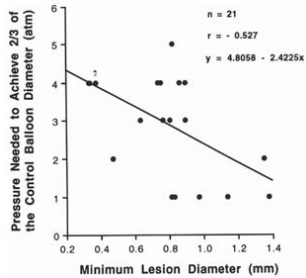

Figure 3. Scattergram showing the relation between the minimal lesion diameter before coronary angioplasty and the pressure during the first inflation needed to achieve two-thirds of the control balloon diameter at 5 atm. This variable provides an estimate of the intrinsic distensibility of the lesions. By this definition, intrinsic distensibility appears to be inversely related to lesion severity. Thus, the smaller the baseline diameter the greater the pressure needed to achieve two-thirds of the control balloon diameter during the initial inflation ($p < 0.05$).

Figure 4. Bar graph demonstrating the effects of sequential low pressure (1 to 2 atm) inflations on vessel distensibility (n = 5). Values shown are mean value ± SEM at each inflation pressure. Sequential low pressure inflations fail to increase segmental (lesion) distensibility, as determined by minimal balloon diameters achieved at 1- and 2-atm balloon inflation pressure. After successful coronary angioplasty at higher balloon inflation pressures (range 5 to 8 atm), there is a marked increase in segmental distensibility (p values comparing first and second inflations to final inflation as shown).

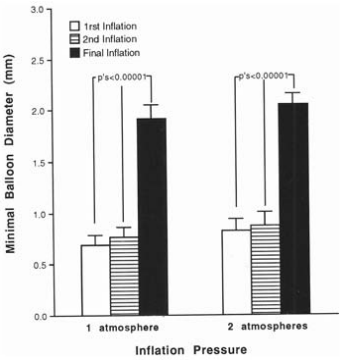

Table 3. Intravascular Ultrasound Data*

Distensibility Index	Plaque Area (mm^2)	Lumen Area Occupied by Plaque (%)
PTCA Site		
22.81	12.10	63.35
8.95	7.86	46.24
10.31	11.14	61.21
12.25	13.57	64.93
12.70	12.0	64.0
22.86	7.4	68.0
13.43	15.0	69.12
Mildly Diseased		
6.66	11.6	44.6
16.66	6.4	55.3
5.36	8.2	36.3
4.08	4.23	21.66
0.43	5.23	24.37
7.41	5.80	33.33
7.60	9.70	40.65
Normal		
14.29	—	—
12.50	—	—
12.35	—	—
16.45	—	—
10.84	—	—
6.73	—	—
11.89	—	—
17.96	—	—

*See text for explanation. PTCA = percutaneous transluminal coronary angioplasty.

damage. In a previous study performed under carefully controlled laboratory conditions, it was demonstrated that relatively severe degrees of stretching (>50% beyond relaxed internal medial diameter) were necessary to induce smooth muscle paralysis in muscular arteries (8). In contrast, it has been estimated that coronary angioplasty more typically results in only 15% to 30% stretching of the media beyond its relaxed diameter (8). These observations suggest that the hypothesis of balloon-induced irreversible medial injury with subsequent smooth muscle paralysis is an unlikely mechanism for lumen improvement after coronary angioplasty.

Arterial distensibility: arteriographic measurements. Previous studies (28,29) have used balloon pressure–diameter relations to try to assess different characteristics of the plaque but not specifically to try to evaluate the changes induced by balloon angioplasty. Our data demonstrate an increase in arterial distensibility after coronary angioplasty at all sequential balloon inflation pressures. The finding of only very small increases in minimal balloon diameters between the first and final balloon inflations in the ex vivo procedures suggest that changes in balloon material distensibility would not explain the large increases in distensibility observed in vivo, particularly at low inflation pressures.

The data from the second cohort of patients with two consecutive inflations at only low pressures (1 and 2 atm) followed by a final sequential inflation (i.e., 1 and 2 atm) provide additional support for the study hypothesis. The lack of change in minimal balloon diameter between the first and second inflations, followed by a large increase in diameter during the low pressure inflation after successful high pressure balloon expansion, suggests that the diseased vessel segment does not increase its distensibility until the cicatrizing effect of the plaque is released by plaque splitting.

In the main cohort of patients of this study the increase in distensibility found during the first and final inflations at different pressures was not homogeneous. The increase in balloon diameters between the first and final inflations, in vivo, were smaller at higher inflation pressures. These variations in the increase of distensibility found at different pressures may have several explanations. First, distensibility curves typically exhibit a steep initial slope followed by a plateau phase at higher pressures. The smaller increases in distensibility at higher pressures found in our study may reflect this plateau phase of the distensibility curve. The most likely explanation, however, is that during the first balloon inflation the diameters achieved were increased by an angioplasty (splitting) effect caused by these higher inflation pressures (4 to 5 atm). Thus, at an inflation pressure of 4 and 5 atm, the first inflation served to increase vessel distensibility rather than merely to measure it. This is a limitation of our study, but, if anything, it may result in an underestimation of the change in distensibility caused by coronary angioplasty. This interpretation is also supported by the data in patients undergoing sequential low (1 to 2 atm) pressure inflations. Another limitation of the study may be that the distensibility of the lesion was measured at pressures higher than physiologic. However, because of the usual morphology of distensibility curves, it is likely that the increases in distensibility would be at least as great at lower pressures than at the pressures at which they were measured. This view is supported by the intravascular ultrasound data, which show that distensibility is measurably augmented after coronary angioplasty at physiologic blood pressures.

Previous studies have found differences in the pressure–diameter relation related to certain lesion morphologic characteristics (29). We did not observe any significant differences in the intrinsic distensibility or the change in distensibility between eccentric and concentric lesions. This may be explained by the observation that eccentric lesions in our series were more severe than concentric lesions (minimal baseline diameter 0.63 ± 0.07 vs. 0.85 ± 0.07 mm, respectively, $p = 0.05$) and that eccentric lesions were more heavily calcified (3 of 9 eccentric lesions were moderately to severely calcified vs. 1 of 15 concentric lesions, $p < 0.01$).

Measurements of arterial distensibility: intravascular ultrasound. Previous data from intravascular ultrasound studies have suggested that variation in vessel circumference during the cardiac cycle is severely impaired in atherosclerosis compared with normal vessels (9,10,13). Reddy et al. (9) have reported a mean lumen area change during a cardiac cycle of 14% in 16 coronary sites in patients without atherosclerosis compared with only a 4% change in 25 mildly diseased coronary sites in patients with atherosclerosis. They observed an intermediate value of 9% in 10 severely diseased segments after balloon angioplasty. They suggested that the diminished response to intraarterial pressure changes that occurred in even mildly diseased arteries indicated decreased arterial distensibility and that coronary angioplasty increased arterial distensibility by producing plaque fracture. The findings of the current study are in agreement with these results. In the eight control segments in our series without any evidence of atherosclerosis by angiography or intravascular ultrasound the mean variation in lumen area during the cardiac cycle was 12.9%, similar to the results reported by Reddy et al. (9). This increase in lumen area probably represents the normal response of a normal vessel to the physiologic changes in blood pressure that occur during the cardiac cycle. In our series, the distensibility indexes of the seven segments evaluated with intravascular ultrasound after coronary angioplasty were not different from those observed in eight coronary segments without detectable coronary artery disease (14.7 ± 2.2 vs. 12.9 ± 1.2, respectively, p = NS) but were significantly greater than those observed in the mildly diseased proximal segments of the balloon-dilated arteries (14.7 ± 2.2 vs. 6.9 ± 1.9 respectively, $p < 0.05$). This was true despite the fact that the plaque index, measured by intravascular ultrasound, was significantly greater in the balloon-dilated segments compared with the proximal sites (0.62 ± 0.03 vs. 0.36 ± 0.04, $p < 0.05$). The observation that even mild degrees of coronary atherosclerosis impair distensibility, along with the negative correlation found between an indirect measurement of the amount of plaque (minimal baseline diameter) and lesion intrinsic distensibility (see Fig. 4), support the hypothesis that atherosclerosis significantly impairs arterial distensibility. These intravascular ultrasound data are consistent with the angiographic data and suggest that coronary artery distensibility significantly increases after balloon angioplasty.

Study limitations. One limitation of this study is that balloon assessment of lesion distensibility and the evaluation of distensibility at physiologic pressures by intravascular ultrasound were not performed in the same patients. Although it could have been useful to perform ultrasound assessment of segmental coronary distensibility before and after angioplasty in the same patients, it was thought that the passage of a 4.3F catheter through a severe stenosis could pose an unacceptable risk to the patients participating in this study. In addition, it was thought that before coronary angioplasty, the large profile of the ultrasound catheter would have obstructed the lumen sufficiently to decrease distending blood pressure, rendering these measurements inaccurate. Finally, the passage of the ultrasound catheter across the stenosis before balloon dilation could disrupt the

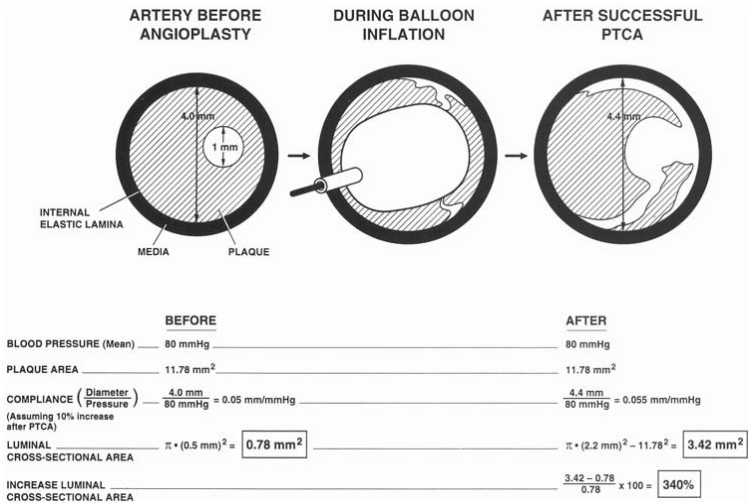

Figure 5. Schematic illustrating the marked increase in lesion/lumen cross-sectional area expected, with modest increases in segmental distensibility. Assuming a 10% increase in segmental distensibility at 80-mm Hg perfusion (mean arterial) pressure after successful plaque splitting, there would be a 340% increase in lumen cross section, assuming that the plaque is completely incompressible and is neither extruded nor embolized. PTCA = percutaneous transluminal coronary angioplasty.

lesion (Dotter effect), making it more difficult to assess the response of the lesion to the first dilation.

It is recognized that angiographic measurement of minimal balloon lumen diameter is a relatively indirect technique for precise determination of the physical characteristics (distensibility) of the underlying arterial segment. For example, in a number of cases the minimal balloon lumen diameter at 1 atm was slightly smaller than the measured postangioplasty minimal lesion diameter. There are several potential explanations for this: 1) Balloon diameter is a measure of the contrast column inside the inflated balloon and fails to take into account the thickness (on two sides) of the balloon material (i.e., two sides of Polyethylene 600 is 0.10 mm thick [Advanced Cardiovascular Systems, personal communication, October 1993]). 2) In cases where there is marked segmental dilation after high pressure (therapeutic) inflations, the minimal lumen diameter at physiologic blood pressure may be larger than the inflated balloon diameter at low pressure such that the balloon does not contact the arterial wall and will underestimate the segmental compliance. 3) The contrast density of Conray 60 used in the balloon is less than that used (Omnipaque 350) during postangioplasty angiography. 4) Small air bubbles in the balloon could lead to underestimation of the balloon diameter, particularly at low pressures. 5) Extraluminal (subintimal) contrast may be detected during the quantitative measurements of minimal lumen diameter after coronary angioplasty, and this may lead to overestimation of the actual diameter mediating the balloon–vessel wall contact. Overall, the minimal lumen diameter of the balloon was only 0.12 ± 0.05 mm smaller than the minimal lumen diameter of the postangioplasty segment at 1-atm balloon inflation pressure and was 0.05 ± 0.04 mm larger than the lesion minimal lumen diameter at 2 atm. Thus, it is possible that the postangioplasty (lesion) segmental distensibility was slightly underestimated by the balloon diameter measurements at 1 atm (i.e., the lumen was larger at a physiologic distending pressure of 70 to 100 mm Hg than at the balloon inflation pressure of 760 mm Hg/1 atm). However, this underestimation appears to be modest and would not alter the main conclusions of this study.

Implications and conclusions. To explain how increased lesion distensibility may account for successful coronary

angioplasty, it is important to recognize that even small changes in segmental compliance may result in important changes in lumen cross-sectional area. In Figure 5 a schematic representation of the possible influence of small increases in distensibility on lumen cross-sectional area is shown. With the assumptions that the plaque is incompressible (1,3), is not extruded along the vessel (1,3) and does not embolize (2), a 10% increase in segmental distensibility at 80 mm Hg mean arterial perfusion pressure would produce a 340% increase in lumen cross-sectional area. Thus, the "release" of the media from the cicatrizing effects of the noncompliant intimal plaque may allow the vessel to passively distend in response to hydrostatic forces (blood pressure) and may be an important mechanism in coronary angioplasty-induced lumen enlargement.

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